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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,212	11/13/2003	Mark Donnelly	GC559-D1	5751

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EXAMINER

RIGGINS, PATRICK S

ART UNIT PAPER NUMBER

1633

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/714,212

Applicant(s)

DONNELLY ET AL.

Examiner

Patrick S. Riggins

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8,12-17 and 21-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8,12-17 and 21-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 November 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>11/13/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Receipt is acknowledged of a Preliminary Amendment file concurrently with the instant application on 11/13/03, in which claims 1-4, 13-17, 22, and 23 were amended and claims 9-11 and 18-20 were canceled. Presently claims 1-8, 12-17, and 21-23 are pending and under examination.

Drawings

2. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because Figure 4 is dark and the numbers at the tops of the lanes are not of sufficient clarity. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

3. The disclosure is objected to because of the following informalities: The Brief Description of the Drawings for Figure 5 on page 4 must refer to the SEQ ID NOs pertinent to the sequences present in Figure 5. Otherwise, Figure 5 will fail to be in compliance with the sequence rules.

Appropriate correction is required.

Claim Objections

4. Claim 7 is objected to because of the following informalities: the claim does not end in a period. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-8 and 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
7. Claim 1 recites that the first nucleic acid is “associated” with the second nucleic acid. The metes and bounds of this limitation are unclear. Does this limitation refer to a fusion protein arrangement? Does this limitation simply mean the nucleic acids are potentially on the same plasmid? Does this mean the nucleic acids are in the same cell? Clearly then the skilled artisan cannot determine the metes and bounds of this limitation in the claim.
8. Claim 3 recites that the nucleic acid encoding the chaperonin is naturally produced. When considered in light of the specification it would seem that this limitation intends that the chaperonin is naturally produced and not the nucleic acid or that the nucleic acid is native to the cell. In the context of claim 1, it is the proteins that are being produced not the nucleic acids. As such the skilled artisan could not ascertain the metes and bounds of this claim.
9. Claims 13 and 14 recite that the first and second nucleic acids are “separated by” a cleavage site with claim 14 reciting that it is a chemical cleavage site. It is unclear how the

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nucleic acid would be linked through a chemical cleavage. Further the specification suggests that it is the separate portions of the encoded fusion protein that are separated by a cleavage site, e.g. with a protease site. Thus, the metes and bounds of these claims are not clear to the skilled artisan.

10. Claim 16 is whole unclear as to its meaning. It is grammatically incorrect and the limitation "under the control of an expression signal capable of overexpression said chaperonin". What does this mean? It would seem likely that this is intended to recite something to the effect of --under the control of a promoter which leads to the overexpression of said chaperonin.--

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1, 3, 6, 17, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Schon-a (Gene 147: 91-94 (1994), newly cited).

13. The claims are drawn to a method of producing a protein where a host cell comprising a first nucleic acid encoding SEQ ID NO: 21 or SEQ ID NO: 22, a second nucleic acid encoding a protein, and a third nucleic acid encoding a chaperonin capable of binding to SEQ ID NO: 21 or SEQ ID NO: 22. The chaperonin can be naturally produced in the host cell which can be bacterial. The claims are further drawn to an expression vector comprising a first nucleic acid

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encoding SEQ ID NO: 21 or SEQ ID NO: 22 and a second nucleic acid encoding a protein.

Finally the claims are drawn to a host cell comprising this expression vector.

14. Schon-a discloses an expression vector encoding GroES from *B. stearothermophilus* which necessarily comprises SEQ ID NO: 22. The expression vector further comprises the kanamycin resistance cassette which necessarily encodes a protein (See Figure 1 and section (b) on page 93). Furthermore, Schon-a discloses the transformation of this plasmid into *B. subtilis* in the presence of kanamycin. Absent evidence to the contrary, GroES from *B. stearothermophilus* would be capable of interacting with GroEL of *B. subtilis*. By culturing the transformed *B. subtilis* in the presence of kanamycin, this ensures that the kanamycin resistance protein would be produced (see Figure 2 and section (c) on page 93). Clearly then, Schon-a discloses all of the limitations of claim 1, 3, 6, 17, and 21.

15. Claims 17 and 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Schmidt (J Bacteriol 174: 3993-3999 (1992), newly cited) as evidenced by the New England BioLabs Catalog (NEB, newly cited).

16. The claims are drawn to an expression vector and host cell as above further where the host cell can be *E. coli*.

17. Schmidt discloses the cloning of the groESL operon from *B. subtilis*. The plasmids pASG145 and pASG241 both comprise the groES gene of *B. subtilis* inserted into pACYC177. Thus each of these plasmids necessarily comprises a nucleic acid encoding SEQ ID NO: 21 which as shown in Figure 2. As page 226 of NEB shows, pACYC177 comprises nucleic acids encoding both kanamycin resistance and β -lactamase, either of which can comprise the second nucleic acid encoding a protein (Figure 1 and Table 1). The plasmid is transformed into *E. coli*.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

19. Claims 1, 2, 5-8, 16, 17, and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amrein (Proc Natl Acad Sci USA 92: 1048-1052 (1995), of record) in view of Schon-b (FEMS Microbiol Lett 134: 183-188 (1995), newly cited) as evidenced by Dale (Protein Eng 7: 925-931 (1994), of record).

20. The claims are drawn to a method of producing a protein in a host cell as described above, where the method can further comprise isolating the protein from the host cell. The nucleic acid encoding the chaperonin can be heterologous to the host cells and can be linked to promoter that can overexpress the chaperonin. The host cell can be *E. coli*. The claims are further drawn to an expression vector and host cells comprising that expression vector as described above.

21. Amrein discloses a method of expressing p50csk by co-overexpressing *E. coli* GroES and GroEL (whole paper). The plasmid pREP4groESL was cotransfected with a plasmid encoding and expressing csk. Thus, as the plasmid encoding GroES (pREP4groESL) is cotransfected with the plasmid encoding csk. Thus these nucleic acids can be considered to have been associated. The GroEL is under the control of the lac promoter/operator and as such can be highly expressed under proper induction conditions (see Figure 1 of Dale). The csk after induction is purified from

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the host cells which are *E. coli*. The GroESL expression plasmid pREP4groESL further comprises the lac repressor gene and the kanamycin resistance gene. Thus providing the second nucleic acid encoding a protein.

22. As Amrein discloses the use of *E. coli* GroES and GroEL, Amrein does not disclose chaperonin binding domains comprising either SEQ ID NO: 21 or SEQ ID NO: 22.

23. Schon-b discloses nucleic acids encoding GroES and GroEL of *B. stearothermophilus*, of which GroES necessarily comprises SEQ ID NO: 22. It would have been obvious to one of ordinary skill in the art to have used the nucleic acid encoding the *B. stearothermophilus* GroES and GroEL as taught by Schon-b in the vectors and methods of Amrein because “the GroE proteins of both bacterial species [i.e. *E. coli* and *B. stearothermophilus*] are functionally interchangeable” (last line of first paragraph of page 186 of Schon-b). One of skill in the art would have been motivated to use the GroE proteins of *B. stearothermophilus* with a reasonable expectation of success because “GroEL from *B. stearothermophilus* is significantly more resistant towards unfolding by heat and by denaturants” and “both operons are functionally interchangeable (page 188, section 4).

24. Claims 1, 3, 4, 6-8, 17, and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No 6,068,991 (effective filing date 12/16/97, hereinafter Liu) in view of Schon-b.

25. Liu discloses and claims expression vectors comprising DNA encoding *E. coli* groES and a heterologous gene sequence, host cells which can be *E. coli* comprising these expression vectors, and a method for producing a protein using these host cells (see claims 1, 2, 10-12, and 17-19). As GroEL is not exogenously supplied, it is the endogenous GroEL that is utilized in the

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method. The expression vectors further comprise genes encoding, for example GCA which is to be expressed. Thus the nucleic acids encoding GroES and GCA are associated.

26. Liu does not disclose using a GroES that comprises SEQ ID NO: 21 or SEQ ID NO: 22.

27. Schon-b discloses nucleic acids encoding GroES of *B. stearothermophilus*, which necessarily comprises SEQ ID NO: 22. It would have been obvious to one of ordinary skill in the art to have used the nucleic acid encoding the *B. stearothermophilus* GroES as taught by Schon-b in place of the *E. coli* GroES in the vectors and methods of Liu because “the GroE proteins of both bacterial species [i.e. *E. coli* and *B. stearothermophilus*] are functionally interchangeable” (last line of first paragraph of page 186 of Schon-b). One of skill in the art would have been motivated to use GroES of *B. stearothermophilus* with a reasonable expectation of success because *B. stearothermophilus* proteins are significantly more resistant towards unfolding by heat and by denaturants (page 188, section 4).

Conclusion

28. No claim is allowed.

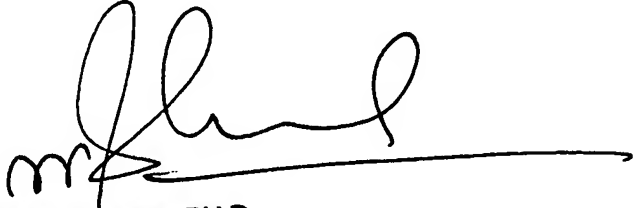
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick S. Riggins whose telephone number is (571) 272-6102. The examiner can normally be reached on M-F 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick Riggins, Ph.D.
Examiner
Art Unit 1633



RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER